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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/871,146	05/25/2001	Anthony E. Bolton	033136-182	8192

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EXAMINER	
CHERNYSHEV, OLGA N	
ART UNIT	PAPER NUMBER
1646	8

DATE MAILED: 07/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/871,146	BOLTON ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-46* is/are pending in the application.

4a) Of the above claim(s) *20-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group II in Paper No. 7 is acknowledged. The traversal is on the ground(s) that there would be no serious burden on the Examiner to examine all the claims due a close relationship between the subject matter of Groups I and II claims. This is not found persuasive because an application may properly be required to be restricted to one of two or more claimed inventions if they are able to support separate patents and they are either independent (MPEP § 806.04 - § 806.04 (j)) or distinct (MPEP § 806.05 - § 806.05 (i)). The Examiner has shown that the Groups are independent or distinct for the reasons in the previous Office action (see Paper No.6). Furthermore, MPEP § 803 provides that the separate classification (i.e., class and subclass) of distinct inventions is sufficient to establish a *prima facie* case that the search and examination of the plural inventions would impose a serious burden upon the Examiner; such separate classification was set forth in the Office action mailed April 16, 2002 (Paper No.6). Therefore, a *prima facie* case for a serious search burden was presented in Paper No.6.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-15 have been cancelled and claims 20-46 have been added as requested in the amendment of Paper No.7.

Newly submitted claims 20-32 are directed to invention that is independent or distinct from the invention originally claimed for the following reasons: claims 20-32 are directed to a method for preparing a pharmaceutical composition for the treatment of neurodegenerative disorders, such method is independent and distinct from the elected invention of Group II, which

is directed to a pharmaceutical composition comprising apoptotic cells, because a product and process of making the product represent patentably distinct inventions if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)).

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 20-32 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 33-46 are directed to a method for treating neurodegenerative disorder and correspond to non-elected Group I. Claims 33-46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 7.

Claims 16-19 are under examination in the instant office action.

Priority

3. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Canada on 05/25/2000. It is noted, however, that applicant has not filed a certified copy of the foreign application as required by 35 U.S.C. 119(b).

Claim Objections

4. Claim 19 is objected to because of the following informalities: "a nuerological" should be "a neurological", perhaps. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 17-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention.

Claims 17-19 are directed to a pharmaceutical composition, which is suitable for administration to a mammalian patient to treat or to effect prophylaxis against neurodegenerative or neurological medical disorders. However, the instant specification fails to provide any guidance on how to make the claimed pharmaceutical composition or a unit dosage composition that would treat a neurodegenerative disorder, thereby requiring undue experimentation to discover how to make and use Applicant's invention, as currently claimed.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the

predictability or unpredictability of the art and, (8) the breadth of the claims. In re Wands, 8 USPQ2d, 1400 (CAFC 1988).

The prior art does not teach or fairly suggest the administration of apoptotic cellular material for the treatment or prophylaxis against neurological or neurodegenerative disorders. The instant specification provides a description of a "novel and unexpected discovery that administration to a mammal of apoptotic cells and/or apoptotic bodies previously prepared ex vivo, can be used in the prophylaxis and/or treatment of neurodegenerative and/or other neurological disorders" (page 4, lines 21-24 of the instant specification). It is stated that "[n]eurodegenerative disorders, including Down's syndrome, Alzheimer's disease and Parkinson's disease, are associated with increased level of reactive oxygen specifies (ROS), certain inflammatory cytokines, including IL-1β" (page 5, last paragraph). Based on the experimental results obtained on mice treated with apoptotic bodies in a physiological solution for contact hypersensitivity, "a Th-1-cell inflammatory disorder which is known to be mediated by inflammatory cytokines" (page 13, lines 5-6), it was concluded that the treatment with apoptotic bodies led to significant reduction in inflammation. Consequently, because of the known imbalance of inflammatory cytokines associated with certain neurodegenerative disorders, such treatment was asserted as being effective in the treatment of "any neurodegenerative or other neurological disorder", including "Down's syndrome, Alzheimer's disease, Parkinson's disease, senile dementia, depression and the like" (page 6, second paragraph).

Neurological and neurodegenerative disorders represent vast number of conditions of different etiology, symptoms and development, ranging from trauma to genetic syndromes, for

example Down's syndrome. While it is true that misbalanced levels of some inflammatory cytokines are characteristic for some of the neurodegenerative disorders, there is no evidence known at this moment or provided by the instant specification that would suggest that all neurological and neurodegenerative disorders can be associated with abnormal levels of inflammatory cytokines, absent evidence to the contrary. One skilled in the art would not have reasonable expectations that oral or intravenous administration of apoptotic bodies would lead to the treatment of a Down's syndrome patient. There is also no basis for prophylaxis of Down's syndrome because it is a known genetic disorder characterized by abnormal triplication of 21st chromosome. Moreover, the instant specification fails to provide any evidence or sound scientific reasoning that would support a conclusion that a described model of contact hypersensitivity is adequate for study or treatment of a neurodegenerative disease. There is no indication in the prior art or the instant specification that would lead to a rational suggestion to extrapolate the results of study of allergic contact dermatitis to the treatment of a neurodegenerative disorder, including disorders with shown cytokine misbalance.

The standard of an enabling disclosure is not the ability to make and test if the invention worked but one of the ability to make and use with a reasonable expectation of success. To practice the claimed invention would require knowledge of how to make a pharmaceutical composition which is effective to treat a neurodegenerative or neurological disorder, and this information is not provided by the instant specification. The instant specification has also failed to provide even a single working example, prophetic or actual, of the claimed pharmaceutical composition that would be shown to be effective in the treatment or prophylaxis of a neurodegenerative disorder. In the absence of this guidance a practitioner would have to resort

to a substantial amount of undue experimentation involving the variation in the amount and duration of administration of apoptotic cells/bodies of the instant invention and in determining a suitable route of administration. The instant situation is directly analogous to that which was addressed in *In re Colianni*, 195 U.S.P.Q. 150,(CCPA 1977), which held that a "[d]isclosure that calls for application of "sufficient" ultrasonic energy to practice claimed method of fusing bones but does not disclose what "sufficient" dosage of ultrasonic energy might be or how those skilled in the art might select appropriate intensity, frequency, and duration, and contains no specific examples or embodiment by way of illustration of how claimed method is to be practiced does not meet requirements of 35 U.S.C. 112 first paragraph".

In view of the lack of teachings and unpredictability of the art set forth earlier, and also the total absence of the working examples, the instant specification is not found to be enabling for a pharmaceutical composition, which is suitable for the treatment or prophylaxis of a neurodegenerative or neurological disorders. It would require undue experimentation and making a substantial inventive contribution for the skilled artisan to discover how to use Applicants' invention as currently claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 16 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Fadok et al. (1992, J. Immunology, Vol.148, No.7, pp.2207-2216, reference #4 of the instant IDS).

Fadok et al. teach irradiated thymocytes (page 2208, section "isolation and apoptosis induction in murine thymocytes"), which were analyzed for percentage of apoptotic cells (40 to 50%), and were kept in a solution of RPMI, which is "an acceptable pharmaceutical excipient, see the definition on page 11, lines 23-25 of the instant specification. Thus, the composition of Fadok et al. anticipates the invention of claims 16 and 18.

Conclusion

7. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (703) 305-1003. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 782-9306 for regular communications and (703) 782-9307 for After Final communications.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December

28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556 or (703) 308-4242. If either of these numbers is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Olga N. Chernyshev, Ph.D.
July 18, 2002 oc

JOHN ULM
PRIMARY EXAMINER
GROUP 1600